REMARKS

Claim 1 has been amended to limit its scope to the halocarbon and/or hydrocarbon nanoparticles of claim 4, which is the elected species. Claim 4 has therefore been canceled. Claim 1 has also been amended to delete "substantially" which obviates one of the outstanding rejections.

Claim 7 has also been amended in response to the rejection for indefiniteness, although the rejection in this context is not completely understood by the undersigned.

Claims 11-31 directed to non-elected inventions have been canceled; however, claims 32-36 which require the same active steps as claim 1 but are based on canceled claims 22, 24, 26, 28 and 30 are added. Thus, no new matter is proposed and entry of the amendment is respectfully requested.

Turning, now, to the Office action itself, applicants have canceled claims to non-elected inventions and have confined claim 1 to the elected species of particles. The rejections under 35 U.S.C. § 112, paragraph 2, are obviated by amendment. As to claim 7, the relevance of variants of a value with respect to its method of measurement does not seem to relate to claim 7 as previously worded. It is assumed that "same composition" is clear since claims 5 and 6 are not objected to. Claim 7 has been spelled-out more thoroughly.

It is believed that the formal rejections are thereby overcome.

The remaining rejection is over the art.

Claims 1-8 were rejected over Kao, *et al., Biochem/Biophys. Acta* (1981) 677:453-461 in view of Lanza, *et al.* (*Circulation* (2002) 106:2842-2847) and Lanza, *et al.* (US2002/0168320).

The Examiner correctly characterizes Kao as describing competition for clearance by the reticuloendothelial system (RES) wherein large unilamellar liposomes (designated REV's) successfully compete with each other for clearance. Thus, as the Examiner correctly points out, the clearance of C^{14} labeled REV's is slowed by the presence of unlabeled REV's which presumably "blockade" the RES.

However, the claims have now been limited to nanoparticles which correspond to small unilamellar liposomes (SUV's). SUV's are nanoparticles as they range from 20-50 nm (page 455); the REV's, however, are microparticles as they range from 0.5-2.0 μ.

Because the claims are now limited to nanoparticles which correspond to the SUV's, it will be apparent that Kao teaches away from the invention as now claimed. As noted on pages 457-458, bridging paragraph, a 24-hour lead time is required for the SUV's to blockade REV clearance. Experiments done at 1 or 4 hours after a loading dose of SUV's show that SUV's administered such short times before administering REV's have little effect on clearance of a test dose of REV's. Only if a loading dose of SUV's is administered 24 hours prior to the test dose of REV's is there a successful blockade.

The claims specifically require simultaneous administration of the carrier (which is the blocking formulation) and the active composition. Since the blockading composition corresponds to the SUV's in Kao, Kao would teach that simultaneous administration of the active composition and the carrier would be unworkable for this type of particle. Rather than suggesting the invention as now claimed, Kao teaches away from it.

With respect to Lanza, the particulate compositions described are indeed the same as the particulate compositions included in the claims. However, since Kao does not teach the present

method as applied to such particles, and teaches away from it, the addition of the Lanza documents is not helpful.

The Office notes that Lanza '320 teaches that the presence of particles with avidin/biotin crosslinks promotes clearance via the reticuloendothelial system. The relevance of this statement is not clear, nor is its meaning *per se*, since all it says is that the rapid clearance of circulating avidin-ligand complexes (no particles) via the RES system is accelerated by avidin crosslinking. This appears to have no bearing on the ability of the simultaneously administered carrier of the invention to reduce the clearance of the active composition.

The foregoing should be sufficient to result in the withdrawal of the rejection; however, applicants further point out that Kao is silent with regard to any kind of targeted particulate formulations which are the subject of the present claims. The targeting agent will affect the behavior of the system components and there is no teaching at all in Kao with respect to targeted particles.

Finally, claims 9-10 were rejected over the same documents in further view of Kerr, *et al.* (*Expert Opinion on Investigational Drugs* (2000) 9:1271-1279). Applicants do not rely on the further limitations of claims 9 and 10 for patentability, but propose that claims 9 and 10 are patentable for the same reason as applied to claims 1-3 and 5-8.

Conclusion

Since Kao teaches that nanoparticles must be administered 24 hours in advance in order to blockade the RES so as to reduce the clearance of a similar composition, Kao teaches away from the

invention as now claimed. The claims as amended thus are patentable over the art. Applicants therefore respectfully request that claims 1-3, 5-10 and 32-36 be passed to issue.

Should minor issues remain that could be resolved over the phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 532512001400.

Respectfully submitted,

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